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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/713,632	KAUVAR ET AL.	
	Examiner	Art Unit	
	Amanda M. Shaw	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/04 4/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I in the reply filed on June 12, 2006 is acknowledged. Accordingly, Claims 1-17 have been examined herein.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that the goal of the method and the final step do not agree. Claims 1-7 are drawn to methods for identifying a desired region of a target nucleic acid to be targeted for observation. However, the claims recite the final step of contacting the target nucleic acid with first and second identification probes. The steps listed in the method do not result in the identification a desired region of a target nucleic acid to be targeted for observation. Therefore, it is unclear as to whether the claims are intended to be limited to methods for identifying a desired region of a target nucleic acid to be targeted for observation or methods for contacting the target nucleic acid with first and second identification probes.

Claims 1-7 are indefinite over the recitation of the phrase "said nucleic acid" in claim 1. It is unclear if the "said nucleic acid" refers to the target nucleic acid or another nucleic acid.

Claims 1-7 are indefinite over the recitation of the phrases "said first oligomer" and "said second oligomer" in claim 1. There is insufficient antecedent basis for these limitations in the claim.

Claim 3 is indefinite over the recitation of the phrase "said first and second labels are different". It is unclear if this means that the particulates (i.e. beads) are different or if the fluorophores on the particulates are different. It is also unclear as to whether the labels are different from one another or different relative to some other unstated label. Additionally there is insufficient antecedent basis for these limitations in the claim.

Claims 8-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that the goal of the method and the final step do not agree. Claims 8-17 are drawn to methods for detecting the presence of a target nucleic acid of known sequences. However, the claims recite the final step of contacting the target nucleic acid with first and second identification probes. The steps listed in the method do not result in detecting the presence of a target nucleic acid of known sequences. Therefore, it is unclear as to whether the claims are intended to be limited to methods for detecting the presence of a target nucleic acid of known sequences or methods for contacting the target nucleic acid with first and second identification probes.

Claims 8-17 are indefinite over the recitation of the phrase "said nucleic acid" in claim 8. It is unclear if the "said nucleic acid" refers to the target nucleic acid or another nucleic acid.

Claims 8-17 are indefinite over the recitation of the phrase "proximal nucleotide sequences". This phrase in considered indefinite because it is not clear as to whether the proximal refers to the relationship between the nucleotide sequences and some other unstated sequences or refers to the relationship between a first sequence to which the first oligomer is specific and second sequence to which the second oligomer is specific.

Claim 10 is indefinite over the recitation of the phrase "said first and second labels are the same". It is unclear if this means that the particulates (i.e. beads) are the same or if the fluorophores on the particulates are the same. Additionally there is insufficient antecedent basis for these limitations in the claim.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-6, 8-9, and 12-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Straume et al (WO 01/027328).

Regarding Claim 1 it is noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." Further, in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999) the court held that if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation." In the present situation, the methods are able to stand alone and the preamble limitation is not accorded patentable weight. Accordingly, the claim language of "a method to identify a desired region of a target nucleic acid to be targeted for observation" merely sets forth the intended use or purpose of the claimed method, but does not limit the scope of the claims.

Straume et al teach a method comprising contacting a nucleic acid sample with a first oligomer probe coupled to a first particulate label and a second oligomer probe coupled to a second particulate label wherein the first probe binds upstream and the second probe binds downstream. Specifically Straume et al teach a method which utilizes oligonucleotide probes which are coupled to particulates (i.e. beads) to identify chromosomal DNA. The method comprises (i) contacting a first oligonucleotide probe/bead composition with a nucleic acid sample; (ii) removing the nucleic acids which did not bind to the first oligonucleotide probe/bead composition; (iii) contacting a

second oligonucleotide probe/bead composition with the remaining nucleic acid sample; (iv) removing the nucleic acids which did not bind to both the first and second oligonucleotide probe/bead compositions; and (v) analyzing the remaining nucleic acid sample (Abstract). Straume et al teach that the preferred chromosome organization for assaying chromosomal DNA for the presence of a nucleotide sequence aberration depends on the number of bases separating the first and second nucleotide sequence types being recognized by the first and second hybridization probes used to identify the aberration (Page 13). In the instant case this is being interpreted as one probe which binds upstream and one probe which binds downstream so as to bracket a region. Straume et al also teach that fluorescent molecules, such as fluorescein and its derivatives, rhodamine and its derivatives, cyanide and its derivatives, dansyl, umbelliferone and acridimium, and chemiluminescent molecules such as luciferin and 2,3-dihydrophthalazinediones, may be attached to the hybridization probe or bead and used as detectable label. It is an inherent property of fluorescent labels that they can be detected using a microscope (Page 20).

Regarding Claims 2 and 9 Straume et al teach that the first and second particulate labels comprise fluorophores. Straume et al also teach that fluorescent molecules, such as fluorescein and its derivatives, rhodamine and its derivatives, cyanide and its derivatives, dansyl, umbelliferone and acridimium, and chemiluminescent molecules such as luciferin and 2,3-dihydrophthalazinediones, may be attached to the hybridization probe or bead and used as detectable label (Page 20).

Regarding Claim 3 Straume et al teach that the method wherein said first and second labels are different. In the instant case this is being interpreted that the particulates (beads) are different. Specifically Straume teach that first probe is coupled to a first bead that is responsive to a magnetic field (M). The magnetically responsive bead enables nucleic acids hybridized to the first hybridization probe to be separated from nucleic acids that do not hybridize to the first hybridization probe. The second probe is coupled to a second bead that is non-responsive to a magnetic field (NM) but may be of different size than the first bead. The magnetically non-responsive bead can then be used as a detectable marker following magnetic separation for those target nucleic acids that have both type 1 and type 2 sequences on the same contiguous molecule (Pages 5-7).

Regarding Claims 5-6, and 12-13 Straume et al teach that the nucleic acid probes hybridize to the target nucleic acid which can be DNA or RNA, single stranded or double stranded, fully purified, or as chromatin or chromosomes (Example 5). Additionally Straume et al teach that the preferred chromosome organization for assaying chromosomal DNA for the presence of a nucleotide sequence aberration depends on the number of bases separating the first and second nucleotide sequence types being recognized by the first and second hybridization probes used to identify the aberration (Page 13). In the instant case this is being interpreted as one probe which binds upstream and one probe which binds downstream so as to bracket a region.

Regarding Claim 8 it is noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the

intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." Further, in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999) the court held that if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation." In the present situation, the methods are able to stand alone and the preamble limitation is not accorded patentable weight. Accordingly, the claim language of "a method to detect the presence of a target nucleic acid of known sequence" merely sets forth the intended use or purpose of the claimed method, but does not limit the scope of the claims.

Straume et al teach a method comprising contacting a nucleic acid sample with a first oligomer probe coupled to a first particulate label and a second oligomer probe coupled to a second particulate label wherein the first probe binds upstream and the second probe binds downstream. Specifically Straume et al teach a method which utilizes oligonucleotide probes which are coupled to particulates (i.e. beads) to identify chromosomal DNA. The method comprises (i) contacting a first oligonucleotide probe/bead composition with a nucleic acid sample; (ii) removing the nucleic acids which did not bind to the first oligonucleotide probe/bead composition; (iii) contacting a second oligonucleotide probe/bead composition with the remaining nucleic acid sample; (iv) removing the nucleic acids which did not bind to both the first and second oligonucleotide probe/bead compositions; and (v) analyzing the remaining nucleic acid

sample (Abstract). Straume et al teach that the preferred chromosome organization for assaying chromosomal DNA for the presence of a nucleotide sequence aberration depends on the number of bases separating the first and second nucleotide sequence types being recognized by the first and second hybridization probes used to identify the aberration (Page 13). In the instant case this is being interpreted that the probes are specific for proximal nucleotide sequences. Straume et al also teach that fluorescent molecules, such as fluorescein and its derivatives, rhodamine and its derivatives, cyanide and its derivatives, dansyl, umbelliferone and acridimium, and chemiluminescent molecules such as luciferin and 2,3-dihydrophthalazinediones, may be attached to the hybridization probe or bead and used as detectable label. It is an inherent property of fluorescent labels that they can be detected using a microscope (Page 20).

Regarding Claim 10 Straume et al teach a method wherein the first and second labels are the same. Specifically Straume et al teach that Cy3 was hybridized to the beads (Example 1). In the instant case "the first and second labels are the same" is being interpreted as the fluorophores on the first and second beads are the same.

Regarding Claims 15 and 17 Straume et al teach that the target nucleic acid of known sequence is derived from an organism wherein the organism is human. Specifically Straume et al teach that the target nucleic acid is extracted from a human chronic myelogenous leukemia cell line (Example 6).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4, 7, 11, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Straume et al (WO 01/027328) in view of Nie et al (US Patent 6060242).

The teachings of Straume et al are presented above.

Regarding Claims 4 and 11 Straume et al do not teach a method wherein the first and second oligomers are peptide nucleic acids.

However Nie et al teach a method which uses at least two different PNA probes which are capable of hybridizing to a nucleic acid sample.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Straume et al by using the peptide nucleic acid probes suggested by Nie because they are an equally effective means for detecting nucleic acids.

Regarding Claims 7 and 14 Straume et al do not teach that the method is performed simultaneously on a multiplicity of target nucleic acids using a multiplicity of identification probes having particulate labels of differing hues coupled to oligomers

comprising sequences complementary to a multiplicity of said upstream and downstream sequences bracketing a multiplicity of such regions.

However Nie et al teach that a plurality of PNA probes can be employed simultaneously to achieve a variety of effects. Several probes targeted for different segments of a single nucleotide sequence can be employed to enhance the reliability of the detection method. Similarly, one probe can target one strand of dsDNA, while another probe can target the complementary strand of dsDNA. In the instant case a "multiplicity of target nucleic acids" is being interpreted as different segments of a single nucleotide sequence. The probes taught by Nie also contain different fluorophores (Columns 5 and 6).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Straume et al so as to have used several probes simultaneously to detect a multiplicity of target nucleic acids in order to have achieved the benefits set forth by Nie of providing a method which allows for the enhancement of the reliability of the detection method.

5. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Straume et al (WO 01/027328) in view of Ward et al (US Patent 6506563).

The teachings of Straume et al are presented above.

Regarding Claim 16 Straume do not teach that the target nucleic acid is derived from an organism wherein the organism is an infectious agent.

However Ward et al teach oligonucleotide probes which are capable of binding chromosomes. The probes taught by Ward are sufficient to permit the characterization of bacteria, viruses and/or lower eukaryotes that may be present in a clinical or non-clinical preparation (Column 2 and 29). In the instant case bacteria and viruses are being interpreted as infectious agents.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Straume et al so as to have used the probes to detect bacterial or viral nucleic acids in order to have achieved the benefits set forth by Ward of providing a method which enables one to asses the presence or absence of infectious agents by employing labeled probes specific for the bacterial or viral sequences.

Conclusion

6. No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634
June 21, 2006

CARLA J. MYERS
PRIMARY EXAMINER